IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327**
THIS DOCUMENT RELATES TO: **ALL WAVE 2 CASES IDENTIFIED IN PLAINTIFFS' EXHIBIT A**	**JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO EXCLUDE DR. MAREENI STANISLAUS' TVT-O GENERAL OPINIONS

Defendants Ethicon, Inc. and Johnson & Johnson (collectively, "Ethicon"), incorporating by reference the standard of review for *Daubert* challenges as set out in *Huskey v. Ethicon, Inc.*, 29 F. Supp. 3d 691, 701–02 (S.D. W. Va. 2014), submit this opposition to Plaintiffs' Motion to Exclude the Testimony of Dr. Mareeni Stanislaus [Doc. 2477] and accompanying memorandum [Doc. 2478] ("Pls.' Memo.").[1]

INTRODUCTION

Plaintiffs have not stated legitimate grounds for exclusion of any of Dr. Mareeni Stanislaus' opinions about Ethicon's TVT-Obturator (TVT-O). Their list of eight putative challenges are largely rote recitations of legal standards devoid of meaningful argument that rely on snippets of testimony while ignoring key aspects of Dr. Stanislaus' opinions and methodology. To the extent Plaintiffs' criticisms have any viability, they are matters for cross-examination, not exclusion under *Daubert*. The Court should deny their motion in its entirety.

[1] *See Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

ARGUMENT AND AUTHORITIES

To begin with, Plaintiffs do not and cannot substantiate their contention that Dr. Stanislaus' opinions "clearly exceed the bounds of her qualifications." Pls.' Memo. at 1. Dr. Stanislaus is a graduate of Stanford University and the University of California San Diego medical school, a board-certified physician in obstetrics and gynecology, and a practicing OB-GYN for nearly 25 years. Ex. A, Curriculum Vitae of Mareeni Stanislaus ("Stanislaus CV"); Ex. B, Stanislaus General Rep. (TVT-O) ("Stanislaus TVT-O Rep.") at 1. As a resident, she served as an Assistant Instructor in the Department of OB-GYN at the University of Pennsylvania School of Medicine from 1993 through 1996. Ex. A, Stanislaus CV. And she has been a clinical instructor at the University of California Davis since 2014, as well as practicing as an OB-GYN physician at Pacific Central Coast Clinics. Ex. A, Stanislaus CV; Ex. B, Stanislaus TVT-O Rep. at 1. She is also a member of numerous medical organizations, including the American College of Obstetricians and Gynecologists, the American Urogynecologic Society, and the American Medical Association. Ex. B, Stanislaus TVT-O Rep. at 1. Her qualifications have led Dr. Stanislaus to serve as a preceptor for vaginal mesh products made by other manufacturers. *Id.*

Dr. Stanislaus was trained in medical school to treat stress urinary incontinence (SUI) surgically, primarily with the Burch colpourethropexy. *Id.* at 5. Demonstrating her familiarity with and reliance on medical literature in her clinical practice, Dr. Stanislaus testified that when the TVT was first introduced, she "waited until there was a wealth of peer-reviewed data surrounding it before adopting into" her practice. *Id.* Since the introduction of the TVT-O—which was based on a modification of the TVT procedure and is "very similar" to the TVT—in 2004, Dr. Stanislaus has performed approximately 150 TVT-O implantations. Ex. C, Stanislaus 7/15/16 Dep. Tr. at 26:23–25. She has had favorable outcomes for her patients with both the

TVT and TVT-O devices. *See* Ex. B, Stanislaus TVT-O Rep. at 5 (describing patients' satisfaction with mesh sling procedures she has performed).

A surgeon with Dr. Stanislaus' experience is allowed to examine the literature and offer opinions regarding safety and efficacy of the TVT-O. *See Tyree v. Boston Sci. Corp.*, 54 F. Supp. 3d 501, 585 (S.D. W. Va. 2014) (permitting board-certified urologist with no stated "design" expertise to testify to the safety and effectiveness of mesh as he had "performed almost 3,000 sling procedures," and "cites numerous studies and academic papers throughout his expert report to support his opinion that the Obtryx is both safe and effective"); *Wilkerson v. Boston Sci. Corp.*, No. 2:13-CV-04505, 2015 WL 2087048, at *24 (S.D. W. Va. May 5, 2015) (rejecting attempt to exclude testimony by an obstetrician-gynecologist on the "safety and effectiveness" of midurethral slings and holding that the clinician's extensive experience implanting the devices "along with his review of the existing literature, provides a reliable basis for his opinions on the safety and efficacy of the Advantage Fit").

Nonetheless, Plaintiffs purport to identify eight ways in which Dr. Stanislaus' opinions "clearly exceed the bounds of her qualifications and are founded on insufficient facts and unreliable methodology." Pls.' Memo. at 1. None states a legitimate ground for exclusion.

I. Dr. Stanislaus Offers Relevant and Helpful TVT-O Specific Opinions. That Those Opinions are Supported in Part by Analysis and Literature About the TVT-R and Mid-urethral Slings Generally is not Grounds for Exclusion. (Pls.' Memo. Sections I and IV)

The claim that Dr. Stanislaus' "literature and experience" are an insufficient foundation for her opinions about the TVT-O specifically (as opposed to the TVT-R and mid-urethral slings generally) does not withstand scrutiny. *See* Pls.' Memo. at 3; *see generally id.* at 3–4, 6–7.

A. Dr. Stanislaus' Experience is Sufficiently "TVT-O-Specific."

As discussed above, Dr. Stanislaus is a 24-year board-certified Ob-Gyn who has treated her patients using the TVT-O approximately 150 times. Ex. C, Stanislaus 7/15/16 Dep. Tr. at 26:23–25. She also has extensive experience and training in other surgical treatments for SUI, including with other TVT products, and so is well qualified to evaluate the comparative safety and efficacy of the TVT-O in her clinical practice. *See* Ex. B, Stanislaus TVT-O Rep. at 5.

If Plaintiffs believe that the decline in Dr. Stanislaus' use of the TVT-O over the past six years (in favor of a mini-sling device) undercuts the credibility of her opinions, they may cross-examine her about that fact at trial. Pls.' Memo. at 3; *see* Stanislaus 7/15/16 Dep. Tr. at 23:20–24:21 (Dr. Stanislaus still considers the TVT-O in the "armamentarium of devices to be used for stress incontinence" but "[r]ecently my patients have been choosing to have the mini sling."). Their criticism, however, does not state a legitimate basis on which to attack her qualifications or exclude her testimony.

B. Dr. Stanislaus Relied on TVT-O-Specific Data From the Literature.

Plaintiffs' contrary assertions notwithstanding, Dr. Stanislaus' methodology for forming her opinions about the TVT-O device included analyzing multiple, published, peer-reviewed studies relevant to the TVT-O device specifically. For example, she cites Lauikainen (2014), which reported on the results of a five-year, multi-center randomized clinical trial[2] which found that 91.7 percent of the TVT-O patients were subjectively satisfied with their treatment. Ex. B, Stanislaus TVT-O Rep. at 9–10 & n.34. She examined Groutz (2011), which showed that the benefits of trans-obturator mesh slings include low morbidity and a short operating time, and that

[2] A "randomized trial, clinical trial, or true experiment, is considered the gold standard for determine the relationship of an agent to a health outcome or adverse side effect." Green et al., *Reference Guide on Epidemiology* at 555, *Reference Manual on Scientific Evidence*, Third Ed. (2011).

of 61 patients available for follow-up, 74 percent had their SUI cured, and another 8 percent reported improvement. *Id.* at 8 & n.28, 9 & n.31. She discusses and relies on Athanasiuo (2014), which contained seven years of data on 124 women implanted with the TVT-O specifically and which reported an 81.5 percent objective cure rate. *Id.* at 10 & n.35; *see also* Ex. C, Stanislaus 7/15/16 Dep. Tr. at 144:20–24. She also analyzed and relied on Liapis (2010) showing an objective cure rate among 111 TVT-O patients of 82.4 percent, as well as Angioli (2010), which reports a low complication rate among TVT and TVT-O patients and a cure rate for the TVT-O patients of 72.9 percent. Ex. B, Stanislaus TVT-O Rep. at 8 & n.28; 8–9 & n.30; *see also id.* at 9–10 & nn.33 & 34.

That Dr. Stanislaus was unable to cite on demand at her deposition "the longest-term TVT-O study that she was aware of," Pls.' Memo. at 3, is hardly grounds for disqualification—Plaintiffs are free to cross-examine her at trial on such matters. *Cf. Trevino v. Boston Scientific Corp.*, No. 2:13-cv-01617, 2016 WL 2939521, at *4 (S.D. W. Va. May 19, 2016) (rejecting plaintiff's challenge to a defense expert who had conducted a thorough review of medical literature, and finding that the expert's alleged failure to consider certain specific studies was a matter for cross-examination at trial).

C. Dr. Stanislaus Also Appropriately Relied on Meta-Analyses and Similar Studies.

Dr. Stanislaus relied on larger meta-analyses and systematic reviews of polypropylene mesh slings generally because these types of studies are "the highest level of scientific evidence"—a characterization that Plaintiffs' motion does not even purport to contradict. *Id.* at

11; *see* Ex. C, Stanislaus 7/15/16 Dep. Tr. at 117:20–23.[3] For example, Dr. Stanislaus analyzed and relied on, among others:

- Ford (2015) in which the authors performed a systematic review of 81 randomized or quasi-randomized controlled trials involving 12,133 women and concluded that "[i]rrespective of the routes traversed [*i.e.* transobturator versus retropubic], [mid-urethral sling operations] are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term." Ex. B, Stanislaus TVT-O Rep. at 11 & n.39.

- Schimpf (2014), a systematic review and meta-analysis by the Society of Gynecologic Surgeons concluding that mid-urethral slings generally may result in lower rates of, among other things, blood loss, postoperative pain, and bowel injury. It further suggested that the decision to use a retropubic versus a transobturator sling should be based on which adverse events are of the greatest concern to the patient, and concluded that transobturator full-length mid-urethral slings like the TVT-O compare very favorably to other surgical treatments for SUI. *Id.* at 11–12 & n.40.

- Funk (2013) which examined data involving 188,454 women who underwent a mid-urethral sling procedure between 2001–2010 and found a nine-year cumulative risk of revision or removal of only 3.7 percent and a nine-year risk of revision or removal due to mesh erosion of only 2.5 percent. *Id.* at 12 & n.43.

Plaintiffs provide no reasoned basis for arguing that Dr. Stanislaus should have limited her analysis only to data and experience relevant to the TVT-O specifically and excluded any data related to other TVT devices or mid-urethral slings generally. Pls.' Memo. at 3, 6–7. As Dr. Stanislaus explained at her deposition, the wealth of data demonstrating the safety and efficacy of TVT devices generally supported her decision as a practicing clinician to start using the TVT-O device:

Q: Did that data also support your decision to start using the TVT-O device?

A: Yes, of course.

Q: And why is that?

[3] As Dr. Stanislaus explained at her deposition, a meta-analysis is "a compilation of high-quality evidence, generally randomized controlled trials, put together to form conclusions based on larger numbers than a single trial could provide." Ex. C, Stanislaus 7/15/16 Dep. Tr. at 117:9–13.

> A: Because it's basically a modification of a surgical technique. So knowing that the TVT was effective and safe with extensive data allowed me to consider an improvement in safety by performing the TVT-O.

Ex. 3, Stanislaus 7/15/16 Dep. Tr. at 127:17–25.

Moreover, all of the TVT devices use the same mesh. *Id.* at 144:11–19; Ex. B, Stanislaus TVT-O Report at 10. If the medical literature does not suggest that the mesh's putative defects identified by Plaintiffs (its alleged cytotoxicity; its alleged propensity to degrade, rope, curl and fray; its alleged small pore size, and so forth) cause clinically significant effects in TVT patients generally, that literature also supports the safety of the TVT-O specifically. Plaintiffs' own experts opine that ***all*** polypropylene mesh used in vaginal pelvic surgery is per se defective because of its inherent characteristics. *See, e.g.*, Ex. D, 2/1/16 Rule 26 Expert Report of Jerry G. Blaivas, M.D. at ¶ 31. Given this inherent defect theory, Plaintiffs' implication that Dr. Stanislaus' opinions about the "clinical safety of the TVT-O device" do not implicate her opinions about "the [mesh] material itself," *see* Pls.' Memo. at 7, is puzzling. If Plaintiffs are now contending that the inherent characteristics of polypropylene mesh have nothing to with the "clinical safety" of the TVT-O, then their own experts' contrary testimony should be stricken.

What these large-scale studies demonstrate (in addition to the safety and efficacy of mesh slings including the TVT-O) is that experts in the field of female urinary incontinence who publish in the peer-reviewed literature choose to study the risks and benefits of mid-urethral slings generally without conducting separate analyses for each individual mid-urethral sling mesh product. This is strong proof that Dr. Stanislaus' methodology of considering data about mid-urethral slings generally—along with the TVT-O-specific data already discussed—is reliable and that her opinions satisfy *Daubert*'s "fit" requirement. Stated differently, the physicians who specialize in treating female urinary incontinence believe that the resulting

"Level 1" data from studying mid-urethral slings generally to be important enough that such data is subjected to peer-review and published in prestigious medical journals in order to guide clinicians—like Dr. Stanislaus—who practice evidence-based medicine. *See* Ex. C, Stanislaus 7/15/16 Dep. Tr. at 121:8–122:7 (Level-1 studies are high in the hierarchy of evidence-based medicine, whereas case reports, observation, and internal company documents like e-mails are "very low" or "the lowest.").

D. Dr. Stanislaus Adequately Explained Her Opinion That the Differences Between Laser- and Mechanically Cut Mesh are Clinically Insignificant.

Plaintiffs' one-sentence criticism that Dr. Stanislaus failed to cite TVT-O studies "that deal specifically with laser-cut mesh," Pls.' Memo. at 3, is disingenuous. It is the very *lack* of literature demonstrating a clinically significant difference in laser-cut versus mechanically-cut mesh that informs (in part) Dr. Stanislaus' opinion that the difference is clinically irrelevant:

> Neither the published medical literature nor my experience using both types of mesh indicates that there is a clinically significant different between laser-cut mesh and mechanically cut mesh. I have used both products in my practice over the past ten years, and have not observed a difference in the way the mesh performs based on the way it was cut. Nor does the peer-reviewed published literature discuss a clinically significant difference between the two. Literature prior to 2006—when only mechanically cut mesh was available—and literature after 2006—when both laser-cut and mechanically cut mesh was available—shows the same excellent efficacy and safety overall.

Ex. B, Stanislaus TVT-O Rep. at 16.

E. Dr. Stanislaus' Appropriately Acknowledges the Similarities and Differences Between the TVT-O and TVT-R Devices.

The Court should reject Plaintiffs' request to exclude Dr. Stanislaus' "TVT-O opinions . . . to the extent that they rely on TVT-R [Ethicon's retropubic TVT device] data." Pls.' Memo. at 7. Plaintiffs protest that Dr. Stanislaus cannot reliably "extrapolate" TVT-R data to the TVT-O because of the devices' different adverse event profiles. Pls.' Memo. at 6–7. But Dr. Stanislaus

acknowledged that very fact. Far from ignoring the data on how these devices differ, Dr. Stanislaus factored that information into her TVT-O opinions, just as she factors the relative advantages and disadvantages of the retropubic approach (using the TVT-R) and the trans-obturator approach (using the TVT-O) into her risk-benefit counseling of real-world patients:

> Q. Okay. So is it fair to say that a higher incidence of groin pain associated with the TVT obturator device is a morbidity that the obturator device has and the retropubic device does not have?
>
> A. Well, that is a true statement. You know, when counseling a patient you have to sort of weigh the relative importance of different morbidities. For example, puncturing a bladder, or a bowel, or a major blood vessel could be a more significant morbidity than, say, a groin pain.

Ex. C, Stanislaus 7/15/16 Dep. Tr. at 102:16–25; *see also* Schimpf (2014) (cited in Ex. B, Stanlislaus TVT-O Rep. at 12 n.40) (decision to use a retropubic versus an transobturartor sling should be based on which adverse events are of the greatest concern to the patient).

In sum, the Court should reject Plaintiffs' claims that Dr. Stanislaus' opinions are not "TVT-O-specific" specific enough, or that her methodology based on her experience and literature analysis is somehow lacking.

II. Dr. Stanislaus' TVT-O Opinions Are Derived from Her Experience and Analysis of Literature. That is a Reliable Methodology, and Her Alleged Unfamiliarity with a Single, Lower-Level Study is a Matter for Cross-Examination, not Exclusion. (Pls.' Memo. Sections II and III)

Plaintiffs' one-paragraph assertion that Dr. Stanislaus did not use a "reliable methodology" is little more than boilerplate. Dr. Stanislaus applied her extensive clinical experience to the question of the TVT-O's safety and efficacy, and explains why that experience supports her opinions on the subject. She analyzed an extensive body of scientific literature, both as to the TVT-O specifically and mid-urethral slings generally. That literature includes

what Plaintiffs do not dispute is the highest level scientific evidence—meta-analyses, systematic reviews, and registry studies.

Plaintiffs' critiques do nothing to undermine the soundness of Dr. Stanislaus' methodology. That she has not previously testified as an expert—and has instead spent her professional career treating women, including by using the TVT-O to alleviate their urinary incontinence—is more reason to credit than to discount the reliability of her opinions. *Cf. Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995) ("That an expert testifies for money does not necessarily cast doubt on the reliability of his testimony, as few experts appear in court merely as an eleemosynary gesture. But in determining whether proposed expert testimony amounts to good science, we may not ignore the fact that a scientist's normal workplace is the lab or the field, not the courtroom or the lawyer's office.").

Plaintiffs offer no authority or reasoned argument that Dr. Stanislaus' opinions are unreliable simply because she consulted colleagues about what to include in her report and relied in part on documents provided by counsel. *See* Pls.' Memo. at 4. Plaintiffs' contention is not grounds for exclusion. Neither is Dr. Stanislaus' inability to immediately recite the contents of every FDA document on her reliance list. *See id.* Dr. Stanislaus explained why she relied on the FDA documents, and the significance of those documents to her opinions—*i.e.*, that the FDA documents confirmed her opinion that the TVT-O is safe and effective, but were of minimal significance to that opinion when compared to the published medical literature. Ex. C, Stanislaus 7/15/16 Dep. Tr. at 53:10–54:1.

As for the charge of cherry-picking, Pls.' Memo. at 5–6, Dr. Stanislaus' report and deposition testimony demonstrates its fallacy. Dr. Stanislaus cited a wealth of medical literature, including multiple high-level meta-analyses, systematic reviews and registry studies. Despite

Plaintiffs' counsel's effort to elicit such an admission from her, Dr. Stanislaus' testimony contradicts Plaintiffs' insinuation that she formed litigation-driven opinions and then selectively discarded contrary medical literature:

> Q: Okay. So how did you go about choosing which materials from this list would be discussed in your report?
>
> A: I wanted to rely on the highest quality of evidence. So principally I chose from the systematic reviews and meta-analyses.
>
> Q: Doctor, would you consider any published peer-reviewed literature that discusses the TVT obturator device as relevant to your opinions in this case?
>
> A: Once again, it would depend on the quality of the evidence.
>
> * * *
>
> Q: So is it fair to say you had your opinions first and then you filled in the report with support for those opinions?
>
> A: Having been in practice for years and gone to medical school and residency as I have had the opportunity to form some opinions, those opinions would have been subject to change had I found contrary information. But, yes, I did have some opinions before I started the report.

Ex. C, Stanislaus 7/15/16 Dep. Tr. at 45:5–16; 48:25–49:9 (objections to form omitted).[4]

In the face of this evidence, Plaintiffs' argument that Dr. Stanislaus failed to consider, or inadequately considered, a single study, *see* Pls.' Memo. at 5–6 (citing Teo (2011)), does not state a valid *Daubert* challenge. Plaintiffs purport to acknowledge that an expert "is certainly not obligated to discuss every available article regarding the product at issue." *Id.* at 6. Yet in the next breath, they attempt to hold Dr. Stanislaus to that very standard. As this Court observed in rejecting a similar argument in *Trevino*, "[i]f there are certain device-specific publications that

[4] For brevity and convenience, Ethicon omits objections in citing deposition testimony. It does not waive any of its objections for purposes of trial.

Dr. Badylak failed to review in preparing his expert report, the plaintiff is free to ask him about those publications on cross-examination." 2016 WL 2939521, at *40.

Moreover, the Teo study on which Plaintiffs place so much significance involved a comparison of the incidence of leg pain in recipients of the TVT-R and TVT-O devices. *See* Ex. C, Stanislaus 7/15/16 Dep. Tr. at 104:22–107:15. Dr. Stanislaus was well aware that the TVT-O had a higher incidence of reported leg pain than the TVT-R—and factored that into both her opinions in this case and her risk-benefit discussions with patients. *Id.* at 102:3–25. Moreover, Dr. Stanislaus explained how she evaluated the relative value of the studies, and why she discounts the Teo study as compared to Level-1 evidence:

> Q. Okay. And, Doctor, are you aware of any literature showing that the TVT-O has higher rates of complications than the 3 percent erosion rate you just mentioned?
>
> A. Oh, yes, there are studies. But, you know, I tried to look at the high-quality studies.
>
> Q. Okay. Doctor, is it your testimony that studies that show a higher than 3 percent rate of complications with the TVT-O are not high-quality studies?
>
> A. No, not -- no, that is not my testimony. I am sure there are some studies that show a higher than 3 percent rate. But I believe the higher quality studies show approximately 3 percent or less rate.
>
> ***
>
> Q. What is higher level evidence, the Teo study or symptomatic reviews in meta-analyses like the Schimpf, Ford, Tommaselli and Ogah systematic reviews that you cited in your TVT-O general report?
>
> A. Of course the systematic reviews and the meta-analyses cited.

Id. at 71:17–72:5; 146:13–18.

In sum, Plaintiffs' perfunctory attack on Dr. Stanislaus' methodology goes nowhere. The Court should reject it.

III. Dr. Stanislaus' Opinion That There is No Reliable Evidence TVT-O Mesh Causes Clinically Significant Effects by Degrading or Deforming *In Vivo* is Based on High-Level Medical Literature, Not Only Her Own Clinical Experience. (Pls.' Memo. Sections V and VII)

Citing this Court's decision in *Tyree*, 54 F. Supp. 3d at 583–85, Plaintiffs accuse Dr. Stanislaus of equating the absence of evidence with "evidence of absence," and move to preclude her from testifying that her experience and the medical literature do not support the proposition that polypropylene mesh used in the TVT-O ropes, curls, or frays. In a similar vein, they argue that her clinical experience is an inadequate foundation for her opinion with respect to the lack of evidence of clinically-significant mesh degradation. Plaintiffs are mistaken on both counts.

First, they distort *Tyree*'s "evidence of absence" observation. There, "BSC's experts []observed certain risk and complications in their practice, which are warned of in the DFU, and therefore deduce that there are no other possible risks or complications that should have been included." *Tyree*, 54 F. Supp. 3d at 584. The Court precluded these opinions on warnings adequacy because the "experts' opinions attempt to encompass all possible risks, none of which they have personally observed." *Id.*

Dr. Stanislaus' opinions about the lack of evidence that mesh reacts in the human body in such a way as to cause clinically significant effects are in a wholly different category. Not only does she have extensive experience with Prolene generally, she has also performed an extensive review and analysis of the relevant medical literature. Dr. Stanislaus relies on this experience and research in forming the opinion that there is not sufficient reliable data to conclude that mesh causes adverse reactions *in vivo*. *See* Ex. C, Stanislaus 7/15/16 Dep. Tr. at 95:22–96:3 (disagreeing that particle loss is a likely cause of pain and noting: "We leave particles of Prolene in patients all the time with Prolene sutures and—I mean, it's just a commonly used material."); *see also id.* at 127:4–9 (Dr. Stanislaus has implanted Prolene sutures many thousands of times);

id. at 153:10–17 (Dr. Stanislaus has used Prolene or Prolene sutures for sacrospinous ligament fixation, multiple vaginal vault suspension procedures, paravaginal defect repairs, and repair of abdominal fascia).[5] Dr. Stanislaus has implanted approximately 150 TVT-O devices, explanted both TVT-O and other mesh sling devices, and has not seen evidence either of (1) degradation, roping, curling, or fraying in explanted mesh, or (2) symptoms in her patients whose mesh slings remain in place that would indicate clinically significant mesh deformation. *See, e.g.,* Ex. B, Stanislaus TVT-O Rep. at 15–16; Ex. C, Stanislaus 7/15/16 Dep. Tr. at 115:4–9; *see also id.* at 77:6–9 (" I have patients now that I have been seeing since 2002, and their meshes are still in place. So [I] presume they are still there working without degradation.").

Furthermore, Dr. Stanislaus backs up her opinions based on clinical experience with her extensive knowledge of the medical literature, including published data on the tensile strength of mesh, and a very recent published abstract in which the authors conclude that "Prolene meshes did not undergo meaningful or harmful degradation in vivo." Ex. C, Stanislaus 7/15/16 Dep. Tr. at 115:5–11 (discussing tensile strength data); 143:4–20 (discussing Ong, White and Thames, "The Myth: In Vivo Degradation of Polypropylene meshes").

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[5] For these reasons, this Court's rulings in *Tyree* and *Bellew* are distinguishable. In those cases, the Court excluded testimony from defense experts who offered opinions that the warnings were adequate merely because they included risks that the experts observed in their own practices. *See Tyree*, 54 F. Supp. 3d at 584 (S.D.W. Va. 2014); *see also* Ex. E, *Bellew v. Ethicon, Inc.*, No. 2:13-cv-22473, Order at 33 (S.D. W. Va. Nov. 20, 2014) [ECF No. 265]. While a single physician's experience may not be sufficient basis for concluding that a risk does not exist, it is sound methodology to rely upon a large pool of scientific literature, combined with extensive clinical experience and the evaluation of many physicians and medical organizations, to support a conclusion that certain risks do not occur, or are generally known, and therefore need not be included in the IFU, as Dr. Stanislaus has done here. The Court's analysis in those cases leads to the conclusion that even "evidence of absence" can be established if the witness in question has in fact looked for the evidence in the right places and has determined it does not exist, *i.e.*, there is "sufficient information and investigation."

Perhaps most significantly, the broad, consistent finding in multiple, high-quality scientific studies of the safety and efficacy of mid-urethral slings, including the TVT-O, by itself provides a sound basis for Dr. Stanislaus' opinion that Prolene mesh used in these devices does not degrade or deform in the human body in such a way as to cause symptoms in patients. As Dr. Stanislaus explains:

> The systematic reviews, meta-analyses, long-term studies, registry studies, and randomized controlled trials regarding mid-urethral slings . . . do not show clinically-significant degradation of Prolene mesh. . . . I have not found possible degradation to be the cause of complications in any of my patients, nor have I seen any clinical studies showing an increase in complications resulting from any degradation. The excellent safety and efficacy reported in the medical literature discussed above, even out to seventeen years after the procedure, is inconsistent with the idea that the mesh is degrading in vivo.

Ex. B, Stanislaus TVT-O Rep. at 16.

This Court has previously found that clinicians experienced with mesh can provide sufficient qualification to offer opinions about "how the product reacts within the body." *Winebarger v. Boston Scientific Corp.*, No. 2:13-cv-28892, 2015 WL 1887222, at *26 (S.D. W. Va. Apr. 24, 2015); *see also Tyree*, 54 F. Supp. 3d at 585 (finding urogynecologist who has performed almost 3,000 sling procedures over the last twenty years qualified to testify that mesh does not shrink, contract, degrade, or cause systemic infection); *Huskey*, 29 F. Supp. 3d at 734 (finding Dr. Johnson qualified to opine as to mesh degradation); *Carlson v. Boson Scientific Corp.*, No. 2:13-cv-05475, 2015 WL 1931311, at *9–19 (S.D. W. Va. Apr. 28, 2015) (finding Dr. Galloway's clinical experience and review of the scientific literature adequately qualified him to opine on polypropylene, including its degradation, leaching, shrinkage, and contraction).

It should do the same here. Dr. Stanislaus may not be qualified to discuss alleged mesh degradation or deformation at the pathological level. *See* Pls.' Memo. at 9 (criticizing Dr. Stanislaus for not asking pathologists about degradation). But she does not purport to offer such

opinions. Instead, drawing upon her own extensive clinical experience actually treating women with mesh slings like the TVT-O, as well as her thorough review of high-level scientific literature, she offers the opinion that the evidence does not support the notion that mesh degradation or deformation causes clinically significant problems in women treated with the devices. The Court should permit her to offer that opinion.

IV. Dr. Stanislaus Opinion About the Relative Safety of Prolene Mesh is Supported by Her Analysis of the Medical Literature.

Plaintiffs' three-sentence challenge to Dr. Stanislaus' opinion about the comparative safety of alternatives to polypropylene mesh for use in the treatment of urinary incontinence (Pls.' Memo. Section VI) should be rejected out-of-hand. The sole basis for their challenge is Plaintiffs' claim that Dr. Stanislaus cited "[n]o source" for her opinions. Once again, her Report directly contradicts this assertion. *See* Ex. B, Stanislaus TVT-O Rep. at 15 n.57 (citing Quemener (2014) and Milani (2012) in support of her opinion that use of Ultrapro mesh for pelvic organ prolapse has been shown to be associated with erosions, dyspareunia and chronic pelvic pain) and n.58 (citing Denis (2004) in support of her opinion that Vypro mesh "has been found to be poorly tolerated in pelvic floor surgery, with high rates of erosion and problems of cicatrisation.").

Moreover, a key element of Dr. Stanislaus' opinions on alternative products is the *lack* of evidence of their safety. *See* Ex. B, Stanislaus TVT-O Rep. at 15 ("I am unaware of any studies demonstrating the safety or efficacy of a mid-urethral sling made of PVDF for the treatment of SUI. . . Furthermore, I am unaware of any of these meshes being cleared or approved by the FDA for use in treating stress urinary incontinence."). Plaintiffs' protest about "sources" is nonsensical when the point, in part, is that after a thorough review of the medical literature, there is a *lack* of safety data for their proposed alternative designs. It is Plaintiffs' burden to establish

the safety and efficacy of their proposed alternative designs, not Defendants. Testimony from defense experts based on extensive experience and research that there is no reliable evidence of safety and efficacy is highly relevant on this issue.

V. Dr. Stanislaus is Qualified to Offer Opinions About the TVT-O IFU.

Based on her experience using the device, and her extensive review of the medical literature, Dr. Stanislaus offers the opinion that "the labeling for the TVT-O device was appropriate for physicians to use the device safely for its intended purposes." *Id.* at 18.[6] Plaintiffs' one-paragraph challenge to this opinion, like several others discussed above, is devoid of meaningful argument and the Court should deny it.

Plaintiffs cite this Court's decision in *Sederholm v. Boston Scientific Corp.*, No. 2:13-cv-12510, 2016 WL 3282587, at *16 (S.D. W. Va. June 14, 2016), for the proposition that an expert "is not qualified to opine on the adequacy of the [IFU] merely based on risks he observed in his own practice." Pls.' Memo. at 10 & n.53. But Dr. Stanislaus does not rely only on her own experience with the TVT-O:

> Warnings regarding carcinogenicity, degradation, contracture/shrinkage, and cytotoxicity would be contrary ***to the high-level clinical literature regarding TVT-O use*** and therefore should not, in my opinion, have been included in the IFU.

Ex. B, Stanislaus TVT-O Rep. at 18 (emphasis added). This alone is sufficient to distinguish the circumstances here from *Sederholm. See Huskey*, 29 F. Supp. 3d at 734–35 (allowing Dr. Johnson to testify about evidence of absence because his opinions were also based on medical literature); *Carlson*, 2015 WL 1931311, at *12. While a single physician's experience may not be sufficient to opine that certain risks do not exist (and do not need to be included in the IFU), it

[6] Dr. Stanislaus also states opinions regarding the Ethicon TVT-O training program she attended, and the TVT-O patient brochures. Ex. B, Stanislaus TVT-O Rep. at 19. Plaintiffs fail to address these opinions and have waived any challenge to them.

is sound methodology to rely upon a large pool of scientific literature and studies, combined with the clinical experience and evaluation of many physicians and medical organizations, to support a conclusion that certain risks do not occur and therefore need not be included in the IFU, as Dr. Stanislaus has done here.

Moreover, as a pelvic surgeon treating female stress urinary incontinence, Dr. Stanislaus is exactly the audience to which the TVT-O IFU is directed. *See* Ex. C, Stanislaus 7/15/16 Dep. Tr. at 85:15–18 ("Q: So you feel like you're an expert in what should and should not be in the TVT-O warnings? A: Insofar as the warnings are directly related to me as a surgeon, yes, I am an expert."). "[D]octors are fully qualified to opine on the medical facts and science regarding the risks and benefits of drugs and to compare that knowledge with what was provided in the text of labeling and warnings." *Winebarger*, 2015 WL 1887222, at *15 (quoting *In re Yasmin & Yaz (Drospirenone) Prods. Liab. Litig.*, No. 3:09–md–02100, 2011 WL 6301625, at *11 (S.D.Ill. Dec.16, 2011)). A physician is qualified to make a comparison between "the risks he perceives that the [device] poses to patients" and whether the labels "convey these risks to physicians." *Id.* (finding Dr. Shull qualified to give opinions on product labeling based on his clinical experience because his testimony did not touch on regulatory issues). Moreover, a physician is qualified to testify about the adequacy of IFUs from a clinical perspective, despite lack of familiarity with FDA regulations and requirements for warnings, or prior experience drafting IFUs. *Id.* at *6–7, 15 (finding Dr. Galloway qualified to provide an opinion on IFUs based on clinical experience despite lack of familiarity with FDA rules or regulations for warnings).

In addition, Dr. Stanislaus is well qualified to testify about the knowledge base of pelvic floor surgeons generally that "all incontinence surgeries carry a potential risk of hematoma, bladder or bowel injury, lower urinary tract infection, vascular injury, infection, urinary

retention, persistent SUI, bleeding, pain, dyspareunia, fistula, de novo urge incontinence, and worsening urge incontinence." Ex. B, Stanislaus TVT-O Rep. at 18. Not only is this opinion within her own experience, Dr. Stanislaus backs her opinion up with a list of published medical articles supporting that opinion. *Id.* at 18 n.66.

Thus, Dr. Stanislaus' opinion that pelvic floor surgeons do not need to be warned about these potential complications in the TVT-O IFU flows directly from, and is amply supported by, her experience ***and*** published literature. *See id.* at 18 ("In my opinion, surgeons do not need to be explicitly warned in the IFU of all of these issues. In 2015, Ethicon updated the adverse reactions section of the TVT-O IFU to include some of these risks. In my opinion, it was not necessary, as the risks are commonly known to experienced pelvic floor surgeons." (footnotes omitted)). The law imposes no duty to warn upon manufacturers for sophisticated users of products with respect to risks that they know or should know. *See, e.g.*, Restatement (Third) of Torts: Product Liability §2 cmt. j (1998); Restatement (Second) of the Law of Torts §402A cmt. j; American Law of Product Liability 3d §32:69 (2016); *Willis v. Raymark Indus., Inc.*, 905 F.2d 793, 797 (4th Cir. 1990). This objective test is not dependent on the knowledge of the individual surgeon, and Dr. Stanislaus is competent to share her opinions about what risks would be obvious to surgeons, and how they would construe the TVT-O IFU given their existing knowledge base.

In sum, if Plaintiffs intend to argue at trial that the TVT-O IFU failed to disclose certain risks, then it is only fair that Ethicon be allowed to defend itself by demonstrating that those risks were obvious to the intended users of the device. Dr. Stanislaus has the training, experience, and knowledge of the peer-reviewed literature to enable her to reliably testify on these matters.

CONCLUSION

For the foregoing reasons, Ethicon respectfully requests that the Court deny Plaintiffs' motion to exclude or limit the testimony of Dr. Stanislaus.

Respectfully Submitted,

BUTLER SNOW LLP

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s/Christy D. Jones
Christy D. Jones
Butler Snow LLP
1020 Highland Colony Parkway
Suite 1400 (39157)
P.O. Box 6010
Ridgeland, MS 39158-6010
(601) 985-4523
christy.jones@butlersnow.com

s/David B. Thomas
David B. Thomas (W. Va. Bar #3731)
Thomas Combs & Spann PLLC
300 Summers Street
Suite 1380 (25301)
P.O. Box 3824
Charleston, WV 24338
(304) 414-1807
dthomas@tcspllc.com

Attorneys for Defendants Ethicon, Inc. and Johnson & Johnson

CERTIFICATE OF SERVICE

I certify that on August 15, 2016, I electronically filed this document with the clerk of the court using the CM/ECF system, which will send notification of this filing to CM/ECF participants registered to receive service in this MDL.

s/ Christy D. Jones

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